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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/742,520	12/20/2000	Ilham Saleh Abuljadayel	674528-2001.2	9656

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EXAMINER
SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
772,520	ABUJA DAYAL
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- [x] Responsive to communication(s) filed on 9/6/02.
- [x] This action is **FINAL.**
- [ ] Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

- [x] Claim(s) 47-72 is/are pending in the application.
- Of the above claim(s) _____ is/are withdrawn from consideration.
- [ ] Claim(s) _____ is/are allowed.
- [x] Claim(s) 47-72 is/are rejected.
- [ ] Claim(s) _____ is/are objected to.
- [ ] Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- [ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- [ ] The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.
- [ ] The specification is objected to by the Examiner.
- [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- [ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).
  - All Some* None of the CERTIFIED copies of the priority documents have been
  - received.
  - received in Application No. (Series Code/Serial Number) _____.
  - received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

- [ ] Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- [ ] Interview Summary, PTO-413
- [ ] Notice of Reference(s) Cited, PTO-892
- [ ] Notice of Informal Patent Application, PTO-152
- [ ] Notice of Draftsperson's Patent Drawing Review, PTO-948
- [ ] Other _____

Office Action Summary

The amendment of 9/6/02 (Paper 9) has been entered. Claims 47-72 are pending and under examination.

The following correction has been entered in the previous Office Action in red ink and initialed and dated by the examiner: In paper 8, page 10, 5th para., changed "47-66 and 68-87" to --47-65--.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: method of increasing the relative number of CD45 low cells in a cell population.

The abstract of the disclosure is objected to because it fails to refer to the invention, as embodied in the claims, of preparing "CD 45 low" cells. Correction is required. See MPEP § 608.01(b).

Regarding claim informalities that were noted in the pervious Office Action (Paper 8, page 10, first paragraph), these have not been addressed by applicant; therefore, the objections of record are repeated.

Claims 57-59 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The HLA-DR receptor of claim 56 inherently has a beta chain with homologous regions. Therefore claims 57-59 fail to further limit claim 56.

Regarding 112, second paragraph rejections of record (Paper 8, page 9), the rejection of is withdrawn claims 63-65, due to the amendment of claim 63.

Claims 47-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 54 "the receptor" lacks antecedent basis. The examiner fails to see how the change in dependency of claim 54 from 53 to 47 overcomes the rejection, since claim 47 recites nothing about a "receptor". It is considered that claim 54 would properly depend from 53, since claim 53 has been amended in its dependency.

The term "low" in claim 47 is a relative term which renders the claim indefinite. The term "low" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant's own disclosure has admitted (page 34, lines 5-6) that the classification of cells as "CD45 low" is arbitrary. Since this classification is "arbitrary" the metes and bounds of the claimed invention are unclear.

Regarding 112, first paragraph, new matter rejections stated in Paper 8, at pages 2-4, the examiner notes the following:

The obtaining of a CD45 low population is deemed supported by the original disclosure --e.g. at Tables 6 and 8.

The new matter rejection of claim 48 is withdrawn, due to applicant's amendment.

Regarding the new matter rejection of claim 52, note the new grounds of rejection stated below.

New matter rejections of record and/or necessitated by applicant's amendment are stated as follows.

Claims 49, 52-62 and 67-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite new matter.

In claim 49 "2 to 24 hours" is new matter. Applicant has urged that Table 6 supports; the examiner finds no support whatever in Table 6; if applicant intended to refer to Table 8, then the examiner finds only support for the discreet variable time points of 2, 6 and 24 hours and not for the full range of continuous variable time points from 2 to 24 hours.

In claim 52, recitation that the "human leukocytes are found in ... bone marrow" is new matter; to the contrary, specification page 28 has taught that "leukocyte progenitors", rather than "leukocytes" are found in bone marrow.

Claim 53 contains new matter because there is no teaching at pages 28-29 that the detected population of CD45 low cells is MHC class I+ or class II+. Applicant has urged that there is support in the general statement that "most undifferentiated and differentiated cells comprise major Histocompatibility Complex class I antigens and/or Class II antigens", as recited at specification page 2, lines 29-31. This vague statement is unconvincing, because also, at page

3, lines 11-17, applicant has referred to numerous stem, progenitor and differentiated cells as DR+ (i.e. positive for an MHC class II antigen), without mention of any MHC class I antigen. Thus there is no support for reciting class I in claim 53. Also, with respect to class II, applicant's vague statement about "most cells" is unconvincing because the particular cells obtained by applicant do not fall within the realm of "most cells". Rather, applicant's CD45 low cells have been treated with an antibody to the beta chain of HLA-DR (class II), which treatment could have caused down modulation of the targeted HLA-DR. Applicant thus has no disclosure bases for reciting either class I or class II in claim 53.

New claims 67-72 all contain new matter because applicant's exemplification of CD45 low cells has not shown that any of his CD45 low cells have these properties. The portion urged by applicant as supporting (page 35, lines 22-30) refers to CD34+ cells, not to CD45 low cells. Applicant's disclosure has not shown that the CD45 low cells also express CD34. Thus there is no basis for applicant to urge (as in paper 8) that "any statements in the specification relating to CD34+ cells may be extraporated to CD45 low cells". The extrapolation is improper, and applicant has no basis for reciting claims 67-72.

Claims 47-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the the genus of agents that "operably claimed invention. The rejections of record

genus of agents that "operably

pertaining to applicant's possession of the engage committed cells" and of the genus of

"biological response modifiers" are maintained.

Applicant has urged that the Rule to 132 declaration of Dr Abuljadayel shows a variety of agents --e.g. as listed in section 4.5 thereof. These results, presented post-filing, are not probative because the description requirement pertains to what the inventor possessed at the time the application was filed, not to what applicant possessed, more than six years thereafter. Further, even the results of the declaration would be unconvincing because one of skill would not readily envision that agents with diverse effects, such as monoclonal antibodies to various and functionally distinct CD antigens, GM-CSF, erythropoietin etc. would have any common effect in producing CD 45 low cells, and from these results one could not envision what the other members of the genus might be. Further the agents listed in part 4.5 of the declaration include agents such as erythropoietin and anti-CD2/CD33 antibodies on magnetic beads, which were not even contemplated in the disclosure. Applicant is thus trying to argue that his genus was originally described by virtue of having later found members thereof which one would not have been directed toward from reading the original disclosure.

With respect to the description of the genus of "Biological Response Modifiers", applicant has urged that Example 4 of the declaration shows use of cortisol. The reference to Example 4 is overly vague without reference to the subsection. Upon a scanning of this document, the examiner can find no specific treating of "cortisol", only of "cyclophosphamide", which is the only BRM exemplified in the original disclosure. Even if both cortisol and

cyclophosphamide were both shown, their art recognized effects are too diverse for one to recognize other members of the genus of modifiers that are to function as applicant wishes. Further, a post-filing date declaration that might show the genus does not how possession "at the time the application was filed", as required by the statute.

Claims 47-61, and 63-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of agents which are antibodies directed to the alpha or beta chan of MHC class I or II receptors, does not reasonably provide enablement for of any agent that operably engages committed cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. As previously stated (Paper 8 pages 6-7), the specification fail to adequately enable one to find agents, other than anti-alpha/beta chain of MHC class I/II antibodies, which operably engage committed cells. See further explanation below.

Claim 63 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for for the use of a biological response modifier that is an alkylating agent, does not reasonably provide enablement for any biological response modifier of committed cells to become CD45 low expressing cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. As previously stated (Paper 8 pages 7-8, the specification fails to adequately enable one to find BRMs other than alkylating agents, which can

be used in conjunction with anti-alpha/beta chan of MHC class I/II antibodies, to transform committed ells into CD45 low cells.

Regarding these two previously stated scope of enablement rejections, the examiner cannot find where applicant's response has specifically addressed there issues, apart from the traversal of the new matter and the lack of possession rejections under 112. The examiner's reasoning set forth in Paper 8 is thus taken as sufficient. To the extent that applicant may consider the 1.132 declaration to overcome the above scope of enablement rejections, the examiner considers these far from sufficient. The fact that applicant might have found additional agents that operably engage committed cells (as listed in section 45) and might have found that cortisol also operates as a BRM (as listed the examiner has no idea where) is insufficient for showing enablement without undue experimentation. As noted supra, under the consideration of the descriptions of the genus, nothing in the disclosure would have led one to particularly consider GM-CSF, erythropoietin or anti-CD2/CD33 antibodies on magnetic beads as agents that operably engage ...", among a myriad of hormones, growth factors, antibodies to cell surface antigens etc. Nothing would have led one to particularly consider cortisol as a BRM among the myriad of immunomodulators, cell surface receptors, cytokines, hormones, nucleic acid sequences, antigens and peptides recited at specification page 14. The examiner cannot even find any mention of corticosteroids therein, as a subgenus.

With the lack of specific direction and only the vague teachings that encompass virtually any biochemical species as an "agent that operably engages" or a BRM, applicant is expecting

one to conduct undue experimentation beyond what was exemplified and/or indicated as allowable in the previous office action.

Claims 47-76 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

As noted in the previous Office action, applicant did not point out a specific utility for the CD45 low cells.

Claims 47-76 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's urgings that the 101 utility and 112 how to use rejections should be withdrawn are based on the 1.132 declaration statement (part 5) that at Feb 2, 1995 one of skill would have known that the CD45 low marker is found in stem cells having a hematopoietic or myeloid nature. This statement is merely self serving and is not based upon any teachings of the specification as filed or upon any extrinsic evidence. Further, since applicant has admitted that the designation of the CD45 marker as "low" is arbitrary, there is no way for one to know whether what the art might have recognized at Feb. 2, 1995 as "CD45 low" is the same as what the applicant has considered to be "CD45 low".

Claims 47-72 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,090,625. Although

the conflicting claims are not identical, they are not patentably distinct from each other because the instant and copending claims are claiming essentially the same process. See rational set forth in paper 8, at pages 10-11.

It is noted in applicant's response, that a terminal disclaimer will be filed, once claims are allowable on other grounds.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday from 8:00 a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

November 19, 2002

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644